

REMARKS**Amendments to the Claims**

Claim 69 has been amended to more particularly point out and distinctly claim that which Applicants regard as their invention. Support for the amendments can be found, for example, on page 12, lines 9-11, and Example 2-4 as indicated by the Examiner (see below). Claim 71 has been amended to render the language consistent with related claims as amended previously. No new matter has been added. Entry of these amendments is respectfully requested.

Rejection of Claims 27, 29, 30, 32, 33, 43, 45, 52, 53, 57, 70-75 and 78-86 Under 35 U.S.C. §112, First Paragraph

Claims 27, 29, 30, 32, 33, 43, 45, 52, 53, 57, 70-75 and 78-86 are rejected under 35 U.S.C. §112, first paragraph. The Examiner states that the Specification does not reasonably provide enablement for the full scope of the claims. The Examiner states that “while being enabling for methods of upregulating heart rate in a mammal by the direct myocardial injection of a construct comprising at least one gene selected from the group consisting of β_2 AR, β_1 AR and $G_{\alpha s}$, the specification does not reasonably provide enablement for methods of upregulating heart rate in a mammal by the introduction of modified cells...” (Page 3 of the Office Action).

Applicants have canceled Claims 27, 29, 30, 32, 33, 43, 45, 52, 53, 57 and 78-86.

Applicants point out that Claims 70-75 are directed to a method of upregulating heart rate in a mammal by introducing a construct by direct myocardial injection. Applicants further point out that the Examiner acknowledges such methods are enabled by the Specification. The Examiner states, “the specification, while being enabling for methods of upregulating heart rate in a mammal by the direct myocardial injection of a construct comprising at least one gene selected from the group consisting of: β_2 AR, β_1 AR and $G_{\alpha s}$...” (page 2-3 of the Office Action) Applicants submit that the scope of independent Claim 70 is entirely within the scope of what the Examiner states is enabled by the Specification, and, therefore, cannot be rejected under 35 U.S.C. §112, first paragraph.

In light of the canceled claims and the Examiner’s own assertion that the Specification is enabling for methods of upregulating heart rate in a mammal by the direct myocardial injection

of a construct comprising at least one gene selected from the group consisting of β_2 AR, β_1 AR and $G_{\alpha s}$. Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejection of Claim 69 Under 35 U.S.C. §112, First Paragraph

Claim 69 is rejected under 35 U.S.C. §112, first paragraph as not being adequately enabled by the Specification. The Examiner states that while the Specification teaches the transient transfection of cultured myocytes, and transient affects of upregulation of heart rate in mammals, the Specification does not enable the permanent upregulation of heart rate in mammals. “Although the specification provides sufficient guidance with regard to upregulating heart rate by the introduction of the constructs containing the β_2 AR gene, the specification fails to provide teachings, guidance, or working examples with regard to *permanently* upregulating heart rate. The working examples provided by the specification clearly show that the observation of increase in heart rate is transient...” (emphasis in original, page 10 of the Office Action).

Applicants have amended Claim 69 to indicate transient upregulation of heart rate, thereby obviating the rejection. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 76 and 77 Under 35 U.S.C. §102(b)

Claims 76 and 77 are rejected under 35 U.S.C. §102(b) as being anticipated by Milano *et al.* (*Science*, 264:582-586 (1994)).

Although Applicants do not accede to the basis for the rejection, in order to facilitate prosecution, Applicants have canceled Claims 76 and 77, thereby obviating the rejection. Applicants reserve the right to prosecute the subject matter of these claims in a continuing application.

Rejection of Claims 76 and 77 Under 35 U.S.C. §102(a)

Claims 76 and 77 are rejected under 35 U.S.C. §102(a) as being anticipated by Drazner *et al.* (*J. Clin. Invest.*, 99:288-296 (1997)).

Although Applicants do not accede to the basis for the rejection, in order to facilitate prosecution, Applicants have canceled Claims 76 and 77, thereby obviating the rejection.

Applicants reserve the right to prosecute the subject matter of these claims in a continuing application.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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